



International Alliance for
Biological Standardization

IABS 3rd Real World Evidence Workshop **“Pragmatic Randomized Controlled Vaccine Trials: Toward Global Alignment on Regulatory Framework and Evidence Standards”**

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Outcome Ascertainment and Validity in Pragmatic Randomised Vaccine Trials

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Pragmatic randomised controlled trials offer opportunities to evaluate vaccine effectiveness and safety under routine healthcare conditions, with outcomes often ascertained through electronic health records (EHRs) and other routinely collected healthcare data. Although randomisation reduces confounding, it does not eliminate bias arising from incomplete or inaccurate healthcare data. The validity of EHR-derived outcomes therefore requires careful consideration, particularly regarding precision and sensitivity. Differences in healthcare-seeking behaviour, data-source coverage, and recording practices may affect the identification of clinical events and introduce differential outcome misclassification between comparison groups.

Drawing on the experience of the Vaccine Monitoring Collaboration for Europe (VAC4EU), this presentation will discuss methodological approaches to identifying and validating clinical outcomes in routinely collected healthcare data. These include the use of standardised clinical definitions, harmonised codelists, and phenotype algorithms to identify outcomes across different healthcare settings and coding systems. Particular emphasis will be placed on outcome validation, including the assessment of positive predictive value (PPV), and how differences in data-source characteristics and healthcare utilisation may influence the accuracy and completeness of outcome identification. While PPV provides information on the proportion of algorithm-identified cases that are true cases, it does not capture events missed by the algorithm. To address this limitation, the SeValid framework will be introduced as an approach to identifying false-negative cases and estimating outcome sensitivity.

The presentation will highlight the importance of fit-for-purpose outcome definitions, understanding data-source diversity, and conducting appropriate validation studies to support reliable interpretation of pragmatic randomised vaccine trials and their use in regulatory decision-making.

